REMARKS

Entry of the foregoing, reexamination, and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.111 and § 1.112, are respectfully requested.

I. Amendments to the Claims

By the foregoing amendment, claim 1 has been amended to recite the subject matter of original claim 9. Claim 4 has been amended to recite that the patient supervenes metabolic acidosis. Support for this amendment may be found throughout the specification as filed, particularly at page 2, lines 29-35. In addition, claim 9 has been canceled without prejudice or disclaimer to the subject matter recited therein. Applicants reserve the right to file at least one continuation and/or divisional application directed to any canceled subject matter. Further, new claim 16 which recites "[a] pharmaceutical composition . . ." has been added so as to correspond with the amendments to the method of claim 1. Support for this amendment can be found throughout the originally filed application. No new matter has been added by the present amendments.

II. Response to Claim Rejections Under 35 U.S.C. § 102

At pages 4-6 of the Office Action, claims 1, 4, and 9 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by JP 10-203961. This rejection is respectfully traversed.

Specifically, the Examiner has stated that JP 10-203961 discloses treating ketoacidosis, without causing alkalosis, by administering a solution comprising the

electrolytes recited in the present claims. According to the Examiner, the electrolyte concentrations recited in the present claims all overlap with the corresponding concentrations disclosed in JP 10-203961 and would have been immediately envisaged by a person of ordinary skill in the art.

Further, the Examiner has indicated that although controlling water balance is not explicitly disclosed in JP 10-203961, such a result would necessarily occur upon administration of the reference electrolyte solution. The Examiner has also stated that ketoacidosis is a type of metabolic acidosis, and could occur in patients under surgical stress. Finally, the Examiner has indicated that controlling acidosis, and administration of the electrolyte solution at 500-8000 ml/day and 60 ml/kg/hr, necessarily requires continuous administration.

As noted above, Applicants have amended the claims to recite a method for controlling water and electrolyte balance and acid-base equilibrium in a patient undergoing an operation or in a postoperative patient.

Moreover, it is well established that for prior art to be anticipatory, every element of the claimed invention must be disclosed in a single item of prior art in the form literally defined in the claim. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 213 U.S.P.Q. 81, 90 (Fed. Cir. 1986). Applicants submit that JP 10-203961 fails to satisfy this requirement, for at least the following reasons.

First, the method disclosed in JP 10-203961 is directed to a patient population that is different than the patient population recited in the present claims. In particular, JP 10-203961 discloses a method for using an electrolyte transfusion solution to amend the water and electrolyte balance in a patient with diabetic ketoacidosis. In addition, the reference does not indicate that the solution disclosed

therein can be used in a patient undergoing an operation or in a postoperative patient. In contrast, the present claims recite a method for controlling water and electrolyte balance and acid-base equilibrium in a patient undergoing an operation or in a postoperative patient.

Second, JP 10-203961 does not disclose the infusion rate recited in the present claims.

For at least the reasons set forth above, the present invention is not taught, either explicitly or inherently, and is thus not anticipated by the cited reference. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

III. Response to Claim Rejections Under 35 U.S.C. § 103

At pages 6-9 of the Office Action, claims 1, 4, 9, and 15 have been rejected under 35 U.S.C. § 103(a) as allegedly upatentable over JP 10-203961 in view of Medline abstract 93060291, HCAPLUS abstract 1984:188290, and HCAPLUS abstract 1997:400035. This rejection is also respectfully traversed.

In particular, the Examiner has relied on HCAPLUS abstracts 1984:188290 and 1997:400035 as establishing that blood gas analysis is used to closely monitor a patient's blood parameters when treating acidosis, and Medline abstract 93060291 as establishing treatment of surgical and postoperative patients with the solution of JP 10-203961. The Examiner has also contended that adjusting infusion speed to maintain a plasma bicarbonate concentration of 22-26 mEq/L is obvious because the normal plasma bicarbonate concentration in humans is 24 mEq/L.

Applicants submit that the subject matter of claims 1, 4, and 9 of the present application is clearly not taught or suggested in JP 10-203961. Additionally, Medline abstract 93060291, HCAPLUS abstract 1984:188290 and HCAPLUS abstract 1997:400035, taken alone or together, do not remedy the serious deficiencies of JP 10-203961.

The present invention provides a method for controlling water and electrolyte balance and acid-base equilibrium in a patient undergoing an operation or in a postoperative patient, by means of continuous infusion of the preparation containing bicarbonate and other electrolytes in a balanced manner, at a ratio of 2 to 60 mL/kg/hour, preferably 5 to 20 mL/kg/hour, and more preferably 5 to 15 mL/kg/hour. The unexpectedly superior effects obtained by the method recited in the present invention are not taught or suggested by JP 10-203961.

Specifically, the method of the present invention supplies bicarbonate *per se* to the human body, thereby promptly correcting acidosis. Furthermore, the patient's water and electrolyte balance and acid-base equilibrium can be controlled by changing the infusion speed or stopping the administration of the preparation, by observing data from blood gas analysis as an index parameter. In other words, the present specification teaches that the rate of the infusion speed of the preparation can be adjusted or the infusion terminated in order to maintain the blood pH in a range of 7.3 to 7.5 and the plasma bicarbonate concentration in a range of 22 to 26 mEq/L.

Accordingly, by administering the preparation of the present invention, the acidosis correction effect is exhibited immediately after the start of infusion and acidosis disappears quickly by stopping the infusion demedication. Therefore, the

preparation of the present invention can be administered safely without inducing metabolic alkadosis during infusion and alkalosis after the stopping of the administration, and without causing problems of hypernatremia.

These superior effects due to the rate of the infusion speed of the preparation of the present invention are not taught or suggested in JP 10-203961.

Additionally, Medline abstract 93060291, HCAPLUS abstract 1984:188290 and HCAPLUS abstract 1997:400035 do not teach or suggest the specific rate of the infusion speed of the preparation of the present invention.

For at least the reasons set forth above, the present invention is not obvious over the combination of references cited by the Examiner. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this Amendment and Reply, or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney by telephone at (703) 838-6609 so that prosecution of the application may be expedited.

Respectfully submitted,

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